



REC'D 04 JAN 2005

WIPO PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY  
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70) **10/541604**

Applicant's or agent's file reference P 65123		<b>FOR FURTHER ACTION</b>		See Form PCT/PEA/416
International application No. PCT/EP2004/000299		International filing date (day/month/year) 16.01.2004	Priority date (day/month/year) 17.01.2003	
International Patent Classification (IPC) or national classification and IPC C07D495/04, C07D295/04				
Applicant KRKA, TOVARNA ZDRAVIL, D.D., NOVO MESTO et al.				
<p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 4 sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> sent to the applicant and to the International Bureau a total of sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (Indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p>				
<p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the opinion</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input type="checkbox"/> Box No. VII Certain defects in the International application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p>				
Date of submission of the demand  17.08.2004		Date of completion of this report  30.12.2004		
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465		Authorized Officer  Baston, E  Telephone No. +49 89 2399-8229 		

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/000299

---

**Box No. I Basis of the report**

---

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.
- ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
  - ☐ publication of the international application (under Rule 12.4)
  - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)
2. With regard to the **elements\*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

**Description, Pages**

1-18 as originally filed

**Claims, Numbers**

1-10 as originally filed

- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing
3. ☐ The amendments have resulted in the cancellation of:
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing *(specify):*
  - ☐ any table(s) related to sequence listing *(specify):*
4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
- ☐ the description, pages
  - ☐ the claims, Nos.
  - ☐ the drawings, sheets/figs
  - ☐ the sequence listing *(specify):*
  - ☐ any table(s) related to sequence listing *(specify):*

\* If item 4 applies, some or all of these sheets may be marked "superseded."

**INTERNATIONAL PRELIMINARY REPORT  
ON PATENTABILITY**

International application No.  
PCT/EP2004/000299

---

**Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

---

1. Statement

Novelty (N)	Yes: Claims	1-10
	No: Claims	
Inventive step (IS)	Yes: Claims	1-10
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-10
	No: Claims	

2. Citations and explanations (Rule 70.7):

**see separate sheet**

**INTERNATIONAL PRELIMINARY  
REPORT ON PATENTABILITY  
(SEPARATE SHEET)**

International application No.

PCT/EP2004/000299

**To section V**

The following documents were cited in the search report and were considered for the examination of the present application:

- D1: GB-A-1 533 235 (LILLY INDUSTRIES LTD) 22 November 1978  
D2: EP-A-0 454 436 (LILLY INDUSTRIES LTD) 30 October 1991  
D3: CALLIGARO, D.O. ET AL.: "The Synthesis and Biological Activity of some known and Putative Metabolites of the Atypical Antipsychotic Agent Olanzapine (LY170053)" BIOORGANIC AND MEDICINAL CHEMISTRY LETTERS, vol. 7, no. 1, 1997, pages 25-30,

The present application deals with a process for the preparation of the CNS-active compound Olanzapine (claims 1-5); furthermore compounds useful as intermediates in this process are claimed (claims 6-10).

Documents D1 (page 10) and D2 (claim 7) anticipate processes which are characterized by a cyclization reaction starting from a phenyl/thienyl amino precursor. In contrast to this the presently claimed process starts from a benzodiazepine intermediate which is subjected to a cyclization reaction using sulfur thus resulting in the formation of the annellated thiophene heterocycle.

Document D3 discloses some derivative of Olanzapine which are not interfering with claims 6-10.

In view of the aforementioned differences novelty is acknowledged for claims 1-10 (Art. 33(2) PCT).

The description contains data which show that the claimed process results in the formation of the desired target molecule in good yield and purity. Thus the involvement of an inventive step is acknowledged (Art. 33(3) PCT).